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Visceral obesity and incident cancer and cardiovascular disease: An integrative review of the epidemiological evidence

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Summary

Evidence shows a strong relationship between obesity, cancer and cardiovascular disease (CVD) risk. However, there is not enough evidence of the role of visceral obesity on both CVD and cancer. Visceral obesity may be more pro-oncogenic than total body fat. Therefore, it is important to know whether abdominal obesity can lead to both CVD and cancer. The present integrative review aimed at evaluating epidemiological evidence on the potential connection of visceral obesity in the occurrence of cancer and CVD. The following databases were searched: SCOPUS, PubMed, Science Direct, Lilacs, SciELO, Google Scholar, Web of Science, Scopus and ProQuest. The presence of visceral obesity can increase the risk of some specific cancer types, but there is controversial evidence about CVD risk based on sex-specific and ageing analyses. There is enough evidence that visceral obesity increases the risk of colorectal, pancreatic and gastro-oesophageal cancer. However, for some types of cancer such as breast, endometrial and renal, visceral obesity is a risk only in post-menopausal women. Regarding prostate cancer, the evidence is controversial. Despite the risk of visceral obesity being consistently associated with CVD in adults, this association disappears in sex-specific and older adults analyses. Moreover, in older adults, the results are controversial due to the use of different measures such as waist circumference and visceral adipose tissue. However, the evidence showing visceral obesity as a risk factor to CVD remains controversial. Sex differences, ageing and body mass index (BMI) category can potentially modify this association. Therefore, further epidemiological studies with analyses stratified by sex and samples including older adults aged 65 and older are needed.

KEYWORDS

aging, body composition, visceral adiposity, waist circumference

1 | INTRODUCTION

Cardiovascular disease (CVD) and cancer are the main leading causes of death globally and the world's major disease burden. CVD continues to be the most prevalent non-communicable disease. There is growing consensus that obesity represents an important risk factor for both of these conditions. Obesity is increasing worldwide, and it is the most prevalent nutrition-related disorder in Western countries.[1]

According to a recent report by the International Agency for Research on Cancer (IARC), which analysed more than 1000 epidemiological studies, there is sufficient evidence to classify obesity, measured by body mass index (BMI), as a causal cause for 13 types of cancers.[2] Similarly, a cohort of 3.5 million adults in the United Kingdom has shown that higher BMI increases risk for coronary heart disease, cerebrovascular disease and heart failure.[3]

However, BMI may not be the most adequate measure to assess obesity, characterized by excessive body weight and fat accumulation. Individuals with the same BMI may have different amounts of body fat and visceral fat. Some people can be classified as normal weight (BMI = 18.5–24.9 kg m^{-2}) as well as with abdominal obesity (waist circumference over than 102 cm in men and 88 cm in women).[1,4,5] Therefore, the impact of adiposity distribution, mostly visceral obesity using sex-specific analyses, needs to be further explored. Despite the vast number of scientific papers on incident CVD and obesity, there are still some questions to be answered. Would an adipose distribution measure be more consistently associated to CVD risk than BMI? Do existing anthropometric measures explain the same CVD risk as the body composition variables measuring visceral adipose tissue? Is the impact of visceral obesity the same in men and women?

Unfortunately, there is not enough evidence for the role of abdominal obesity on cancer and CVD. Evidence of the effect of visceral obesity on the occurrence (incidence or prevalence) of both cancer and CVD in the same study is also scare.[6–8] Visceral obesity can be more pro-oncogenic than total body fat and is related to cardiometabolic conditions such as insulin resistance, diabetes, metabolic syndrome, hypertension and dyslipidaemia.[9] Therefore, it is relevant to explore whether abdominal obesity can lead to both CVD and cancer, independently of total adiposity or BMI category. The objective of this study is to evaluate the epidemiological evidence on the association between visceral obesity and the incidence of cancer and CVD.

2 | METHODS

An integrative literature review was conducted. Observational studies, clinical trials and reviews exploring the role of visceral obesity on the occurrence of cancer and CVD were included. We considered as CVD the group of heart and blood vessels disorders including hypertension, coronary heart disease, cerebrovascular disease, peripheral vascular disease, heart failure, rheumatic heart disease and cardiomyopathies.[4]

Currently, various studies are using BMI as a synonymous of adiposity measure. However, they measure different dimensions. We clarify in our review the differences between BMI, adiposity and visceral fat/obesity. BMI measures the excess of weight per height, but it is not the same of adiposity, which means the excess of body fat. Regarding visceral fat or visceral obesity, there are more appropriate anthropometric measures to evaluate it, such as waist circumference (WC), hip circumference (HP) and waist-hip ratio (WHR). There are also body composition methods to analyse visceral fat or total body fat, such as computed tomography and ultrasound.

An electronic search was performed using the following databases: SCOPUS, PubMed, Science Direct, Lilacs, SciELO, Google Scholar, Web of Science, Scopus and ProQuest. No language or year of publication restrictions were imposed. We analysed both titles and abstracts to decide whether a study could be included in our review. Articles were included if they fulfilled the following criteria: being peer-reviewed and/or research-based, investigating the association in adults and/or older adults and met the search criteria. Studies with incomplete data were excluded.

We described and analysed the evidence from epidemiological studies focusing on visceral obesity as a potential risk factor for both cancer and CVD. Preference was given to well-conducted observational epidemiological studies, mainly case–controls and cohort studies, that evaluated as outcome the incidence of cancer in general, specific types of cancers (breast, prostate, endometrial and others) and/or CVD. Few systematic reviews[10–15] and umbrella reviews[16,17] about both outcomes were also found.

3 | RESULTS

We summarized the evidence in two tables. Table 1 shows the association between visceral obesity with specific types of cancer, and Table 2 displays the association between visceral obesity with CVD. We highlighted in dark grey the non-significant associations between visceral obesity with cancer and/or CVD and in light grey protective significant associations.

In some of the included studies, visceral obesity was not the main independent variable (Tables 1 and 2), but it was instead included as a confounder variable or used as part of a group of variables to define/diagnosis the main independent variable such as metabolic syndrome (MetS).[10,18–21] However, visceral obesity is more appropriate to investigate obesity-related health risks. Therefore, it was challenging to explore the role/connection of visceral obesity with both CVD and cancer. Only one epidemiological study, that is, the Framingham cohort, analysed the relationship between visceral obesity and both CVD and cancer.[6] Other cohort studies analysed the risk of CVD in cancer patients, for example, breast cancer. This is called cardio-oncology field,[22] a new cross-disciplinary field aiming to mitigate CVD morbidity and mortality in cancer patients.

MetS has been consistently associated with the risk of CVD, and recently, some studies investigated its association with several types of cancers, showing also a positive association.[10,18–20] The prevalence of MetS is increasing worldwide and, consequently, the number of studies on its association with health outcomes. Some of the MetS components such as abdominal obesity, diabetes, hypertension and hyperlipidaemia had been associated with CVD and different types of cancer, most of them being sex specific.

3.1 | Evidence on the link between visceral obesity and the incidence of overall and specific types of cancer

A few prospective studies have investigated the association between multicancer sites and visceral adiposity. Two cohorts, one in Europe and another in the United States,[6,23] analysed the association

TABLE 1 Epidemiological evidence on the association between visceral obesity and incidence of specific types of cancer in adults and/or older adults

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
Overall cancer					
Britton (2013)[6]	Cohort Framingham Heart Study (*n* = 3086, 49% women, mean age 50.2 years Followed 5.0 years	Incident of cancer Cancers were validated using medical records (pathology reports). Nonmelanoma skin cancers were not included.	Visceral adipose tissue (VAT) by computed tomography (CT)	After adjustment for clinical risk factors and general adiposity/BMI. VAT was associated with cancer HR = 1.43 (1.12–1.84). Women HR = 1.27 (0.88–1.82) Men HR = 1.43 (1.06–1.94)	VAT Overall—risk Women—NS Men—risk
Liu Y. (2016)[24]	Cohort 68 253 Chinese women	Overall cancer Major site-specific cancers: postmenopausal breast cancer, endometrial, liver and ovarian	Waist-hip ratio (WHR)	WHR was not associated with cancer risk after adjustment.	WHR Overall—NS
Lee (2018)[61]	Cohort 22.9 million Korean adults 769 871 cancer cases Followed 7 years	23 of the most common cancers	WC—quintiles of the cohort	Positive association with 18 of 23 types of cancer varying by sex Adjust for BMI removed some association (premenopausal and postmenopausal uterus and ovary, postmenopausal breast and leukaemia)	WC Overall—risk Women—risk Men—risk 18 cancer—risk
Staunstrup (2019)[23]	Prospective Epidemiological Risk Factor (PERF) cohort 4679 Danish postmenopausal women	Cancer diagnoses were extracted from the Danish Cancer Registry. Overall cancer Site specific cancers	Central obesity defined—trunk-to-peripheral fat ratio, calculated by fat mass in the trunk area/fat mass in arms and legs evaluate by dual-energy X-ray absorptiometry scanners High central obese—quartile 4	Adjusted to BMI Overall cancer HR = 1.50 (1.20–1.88) Site-specific cancers: Respiratory (Q1 vs. Q4) HR = 2.01 (1.17–3.47) Gastrointestinal (Q1 vs. Q4: HR = 1.55 (0.99–2.41) Female genital organs (Q1 vs. Q4) HR = 1.95 (1.00–3.78)	Trunk-to-peripheral fat ratio Overall—risk Overall—NS (gastrointestinal)
Kyrgiou (2017)[16]	Umbrella review of systematic reviews and meta-analyses of observational studies	Colon cancer Pancreatic Breast premenopausal Breast postmenopausal Endometrial Ovarian Lung Melanoma Non-Hodgkin lymphoma Multiple myeloma Leukaemia Oesophageal adenocarcinoma Gastric Biliary tract	Waist circumference (WC) per 10 cm WHR per 0.1 units Continuous scale to measure adiposity	Colon WC HR = 1.25 (1.15–1.35) WC men 1.33 (1.18–1.50) WC women 1.16 (1.08–1.23) WHR HR = 1.29 (1.17–1.43) Men 1.43 (1.19–1.71) Women 1.20 (1.08–1.33) Pancreatic cancer WC 1.11 (1.05–1.18) WHR 1.20 (1.09–1.31) Endometrial WC 1.27 (1.17–1.39) WHR 1.21 (1.13–1.29) Ovarian	WC Overall—risk Women—risk Men—risk WHR Overall—risk Women—risk Men—risk Ovarian and all other sites—NS

(Continues)

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
		Thyroid 36 cancer sites and subtypes were examined.		WC 1.06 (1.00–1.12) WHR 1.00 (0.93–1.07) All other sites are not associated.	
Colorectal cancer					
Chan (2007)[28]	Case–control Patients in Hong Kong, China, recruited after coronary angiography for suspected CAD. Age- and sex-matched control was recruited from the general population (n = 207).	Colorectal neoplasm Assessed by colonoscopy. Advanced colonic lesion was defined as presence of cancer or adenomas.	WC Men ≥ 91.4 cm Women ≥ 81.3 cm	WC OR = 2.29 (1.29–3.72)	WC Overall—risk
Yamaji (2009)[25]	Case–control study 50–79 years old Screening in Tokyo, Japan 782 cases and 738 controls	Colorectal adenoma	Visceral fat area (VFA)—cm^2 by CT	OR = 1.58 (1.11–2.24) for men and women combined, independently of body mass index.	VFA Overall—risk
Knag (2010)[30]	Case–control study 4276 subjects, Koreans that presented for health check-ups	Colorectal adenoma	VAT by CT Highest quintile vs. lowest quintile WC male > 90 cm, female > 80 cm	VAT Adjusted (OR) = 3.09 (2.19–4.36) WC Adjusted OR = 1.66 (1.38–1.99)	VAT Overall—risk WC Overall—NS
Tae-Hoon (2008)[29]	Prospectively enrolled 200 asymptomatic adults, Seoul, Korea, 133 males, 67 females. Mean age, 50.9 8.5 years follow-up	Colorectal neoplasm	VAT by CT 136.61 cm^2 versus VAT under 67.23 cm^2 WC > 90 cm	After adjustment VAT OR = 4.07 (1.01–16.43) WC OR = 2.05 (0.63–6.70)	VAT Overall—risk WC Overall—NS
Keum (2015)[26]	Meta-analysis of observational studies 12 studies included 2776 cases	Colorectal adenomas	VAT—each 25 cm^2 increase Range of VAT area = 30–228 cm^2)	VAT OR = 1.13 (1.05–1.21)	VAT Overall—risk
Abar (2018)[27]	Systematic review of prospective studies 50 936 cases among 7 393 510 participants	Colorectal cancer (CRC)	WC per 10 cm WHR per 0.1 unit	WC HR = 1.02 (1.02–1.03) WHR HR = 1.03 (1.01–1.05)	WC and WHR Overall—risk
Prostate cancer					
Blanc-Lapierre (2015)[10]	Population-based case–control study 1937 men with incident prostate cancer, aged ≤75 years, diagnosed across hospitals, Montreal, Canada 1995 controls The Prostate Cancer & Environment Study (PROtEuS)	Prostate cancer Aggressiveness of PCa—defined by the Gleason score	WC cut-off of 102 cm for abdominal obesity	Cases had similar WC (98.6 vs. 98.5 cm) OR = 0.70 (0.60, 0.82) after considering potential confounders negative association did not vary according to PCa aggressiveness	WC Overall—protective
	Cohort	Prostate cancer	WC per 5 cm	WC	WC and WHR

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
Pischon (2008)[17]	29 502 men without cancer at baseline from eight countries of the European Prospective Investigation into Cancer and Nutrition (EPIC) Follow-up of 8.5 years		WHR per 0.1 unit	RR advanced prostate cancer = 1.06 (1.01–1.1) WHR RR = 1.21 (1.04–1.39)	Overall—risk
De Nunzio (2016)[18]	584 clinic patients Italy Patients with moderate/high cardiovascular risk evaluated for prostate cancer diagnosis.	Prostate cancer diagnosis at biopsy. Secondary end point High-grade disease—Gleason score of ≥ 7	WC Men > 102 cm Women > 88 cm	WC was not associated with prostate cancer (p = 0.669). WC was associated with Gleason score (p = 0.028). Highest WC between Gleason score ≥ 7	WC Overall—NS
Breast cancer					
Agnoli (2010)[32]	Case–control study postmenopausal women, ORDET cohort. Follow-up 13.5 years Cases: 163 women Four matched controls per case	Breast cancer postmenopausal	WC > 86 cm	WC Adjusted RR = 1.23 (0.83–1.81)	WC Women—NS (post)
Agnoli (2015)[19]	Case-cohort study 22 494 women 593 breast cancer cases EPIC—Italian centres European Prospective Investigation into Cancer and Nutrition Followed up 15 years	Breast cancer (BC) Postmenopausal and premenopausal	WC > 80 cm	Whole cohort HR = 1.07(0.82–1.39) Premenopausal 0.77 (0.51–1.16) Postmenopausal 1.04 (0.69–1.57)	WC Women—NS (pre and post)
Bandera (2015)[33]	Case–control, AMBER Consortium, African American (AA) women Cases: 2104 ER+, 1070 ER– cases (including 491 TN cases) 12 060 controls	Breast cancer Premenopausal and postmenopausal Categorized according to hormone receptor status ER+, ER– and TN (ER–, PR– and HER2–)	WHR	Premenopausal ER+ tumours OR = 1.35 (1.01–1.80) Postmenopausal all tumour subtypes combined OR = 1.26 (1.02–1.56).	WHR Women risk (pre and post)
Park (2017)[34]	Cohort Sister Study, nationwide prospective cohort 50 884 participants aged 35 to 74 years old	Breast cancer Premenopausal and postmenopausal	WC (88 cm) WHR (0.85)	Premenopausal with normal BMI WC—NA WHR HR = 1.52 (0.89–2.61) Postmenopausal with normal BMI WC HR = 1.58 (1.02–2.46) WHR HR = 1.38 (1.02–1.85) Premenopausal with BMI ≥ 25 (overweight/obese)	Women Normal BMI WC and WHR—NS (pre) WC and WHR—risk (post) BMI ≥ 25 WC and WHR—NS (pre) WC and WHR—risk (post)

(Continues)

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
				WC HR = 0.74 (0.54–1.01) WHR HR = 0.91 (0.62–1.33) Postmenopausal with BMI ≥ 25 WC HR = 1.43 (1.24–1.66) WHR HR = 1.49 (1.26–1.76)	
Chen (2016)[11]	Meta-analysis of prospective studies	Breast cancer Premenopausal and postmenopausal	WC per 10 cm WHR per 0.1 unit	Premenopausal BC—adjusted RRs WC RR = 1.05 (0.99–1.10) WHR RR = 1.07 (0.95–1.21) Postmenopausal BC WC RR = 1.06 (1.04–1.09) WHR RR = 1.06 (0.99–1.13)	Women WC—risk (post) WC—NS (pre) WHR—NS (pre and post)
Endometrial cancer					
Amankwah (2013)[38]	Population-based case–control study 524 cases 1032 controls Alberta, Canada	Endometrial cancer	WC HP WHR	WC > 84.8–96.0 OR = 2.34 (1.59–3.43) WC > 96.0 OR = 4.21 (2.90–6.10) HP > 104.7–112.7 OR = 1.48 (1.03–2.11) HP > 112.7 OR = 2.87 (2.05–4.00) WHR > 0.81–0.86 OR = 1.86 (1.28–2.69) WHR > 0.86 OR = 2.57 (1.80–3.67)	Women WC—risk HP—risk WHR—risk
Reeves (2011)[35]	Cohort Women's Health Initiative 86 937 postmenopausal women 7.8 years of follow-up	Endometrial cancer	WHR	WHR HR = 1.33 (1.04–1.70)	Women WHR—risk
Sponholtz (2016)[37]	Cohort 47 557 participants the Black Women's Health Study	Endometrial cancer	WC ≥ 88 cm HC highest quartile WHR ≥ 0.85	After adjustment WC RR = 1.09 (0.75–1.58) HC RR = 0.86 (0.55–1.36) WHR RR = 1.06 (0.79–1.42)	Women WC—NS HC—NS WHR—NS

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
Aune (2015)[12]	Systematic review and meta-analysis of prospective studies 22 320 cases among 6 445 402 participants	Endometrial cancer	WC per 10 cm HC 10-cm increase WHR per 0.1 unit	WC 1.27 (1.17–1.39) HC 1.30 (1.19–1.41) WHR 1.21 (1.13–1.29)	Women WC—risk HC—risk WHR—risk
Raglan (2019)[36]	Umbrella review analysed systematic reviews or meta-analyses of observational studies	Endometrial cancer	WHR 0.1 unit	Premenopausal women RR = 1.21 (1.13–1.29)	Women WHR—risk
Pancreatic cancer					
Luo (2008)[40]	Cohort 138 503 women followed for 7.7 years Women's Health Initiative in the United States	Pancreatic cancer	WC per 10 cm WHR per 0.1 unit	WC 1.08 (0.98–1.18) WHR 1.32 (1.12–1.56)	Women WC—NS WHR—risk
Genkinger (2011)[39]	Analysis of 14 cohort studies on 846 340 individuals 2135 individuals were diagnosed with pancreatic cancer	Pancreatic cancer	WHR Highest versus lowest quartile	RR = 1.35 (1.03–1.78)	Overall WHR—risk
Aune (2012)[13]	Systematic review and meta-analysis of prospective studies	Pancreatic cancer	WC 10-cm increase WHR 0.1-unit increment	WC RR = 1.11 (1.05–1.18) WHR RR = 1.19 (1.09–1.31).	Overall WC—Risk WHR—risk
Gastro-oesophageal cancer					
Du (2017)[14]	Systematic review and meta-analysis of prospective studies Total of 2130 gastro-oesophageal cancer cases diagnosed among 913 182 participants	Gastro-oesophageal cancer: total gastro-oesophageal cancer, gastric cancer and oesophageal cancer.	WC WHR	Gastro-oesophageal cancer WC RR = 1.68 (1.38–2.04) WHR RR = 1.49 (1.19–1.88) Gastric cancer WC RR = 1.48 (1.24–1.78) WHR RR = 1.33 (1.04–1.70) Oesophageal cancer WC RR 2.06 (1.30–3.24) WHR RR = 1.99 (1.05–3.75).	Overall WC—risk WHR—risk
Steffen (2015)[42]	European Prospective Investigation into Cancer and Nutrition (EPIC) study 11 years of follow-up 391 456 individuals	Oesophageal adenocarcinoma (EAC) Gastric cardia adenocarcinoma (GCC) Gastric noncardia adenocarcinoma (GNCC)	WC—highest versus lowest quintile HC—highest versus lowest quintile WHR—highest versus lowest quintile	EAC Adjusted for BMI WC HR = 3.76 (1.72–8.22) HC	Overall WC—risk HC—protection WHR—risk

(Continues)

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
				HR = 0.35 (0.18–0.68) WHR HR = 4.05 (1.85–8.87) GCC WC (HR = 1.91 (1.09–3.37) HC (HR = 0.38 (0.42–1.13) WHR HR = 1.95 (1.12–3.38) GNCC WC HR = 1.25 (0.75–2.08) HC HR = 0.69 (0.41–1.15) WHR HR = 2.05 (1.19–3.52)	
O'Doherty (2012)[41]	Prospective NIH–AARP cohort 218 854 participants	Oesophageal adenocarcinoma (EAC) Gastric cardia adenocarcinoma (GCC)	WC WHR	WC EAC HR = 2.01, CI 1.35–3.00 GCC HR = 2.22, 1.43–3.47) WHR EAC HR = 1.81, CI 1.24–2.64) GCC not associated	Overall WC—risk WHR—risk (EAC) WHR—NS (GC)
Renal cancer					
Luo (2007)[15]	Cohort Women's Health Initiative 7.7 years of follow-up 140 057 postmenopausal women aged 50–79 years	Renal cell carcinoma	WHR—highest vs. lowest quartile	RR = 1.8 (1.2–2.5)	Women WHR—risk
Pischon (2006)[43]	European Prospective Investigation into Cancer and Nutrition (EPIC)—eight countries 348 550 men and women 6.0 years of follow-up	Renal cell carcinoma	WC (≥102 cm in men; ≥88 in women) HC quintile WHR quintile	Multivariable adjustment Women WC RR = 1.80 (1.18–2.75) HC RR = 1.65 (0.64–4.23) WHR RR = 1.01 (0.54–1.89) Men WC RR = 1.19 (0.98–1.97) HC RR = 0.44 (0.20–0.98) WHR RR = 1.86 (0.97–3.56)	Women WC—risk HC—NS WHR—NS Men WC—NS HC—protective WHR—NS
Nam (2019)[44]	23 313 046 Korean adults 5.4 years of follow-up, 18 036 cases	Kidney cancer	WC per 5 cm WC male ≥ 100.0, female ≥ 95.0	HR increased with increasing waist circumference (WC) (*p* for trend < 0.001) WC per 5 cm Adjusted HR = 1.09 (1.08–1.11)	Overall WC—risk

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
				WC male ≥ 100.0, female ≥ 95.0 Adjusted HR = 1.18 (1.09–1.28)	
Several types of cancer					
Montella (2015)[20]	Case–control study Italy—hospital-based 690 incident UCB 665 controls	Bladder cancer Urothelial carcinoma of the bladder (UCB)	WC ≥94 cm for men ≥80 cm for women	Bladder cancer OR = 1.63 (1.22–2.19) UCB OR = 1.63 (1.22–2.19)	Overall WC—risk
Britton (2008)[47]	European Prospective Investigation into Cancer and Nutrition (EPIC), 371 983 cancer-free individuals. 8.5 years of follow-up, 1219 histologically confirmed incident cases	Hodgkin's lymphoma (NHL) and multiple myeloma (MM)	WC ≥ 102 cm men, ≥88 cm women WHR ≥ 0.95 men, ≥0.80 women Sex-specific analyses	Visceral obesity was not associated with NHL and MM in men and women. Men—multivariate WC RR = 1.19 (0.91–1.56) WHR RR = 1.12 (0.91–1.36) Women—multivariate WC RR = 0.98 (0.74–1.29) WHR RR = 0.93 (0.77–1.13)	Men WC—NS Women≥NS
Schlesinger (2013)[46]	European Prospective Investigation into Cancer and Nutrition study 359 525 men and women in the follow-up of 8.6 years	Hepatocellular carcinoma (HCC), intrahepatic (IBDC) extrahepatic bile duct system cancer (EBDSC including gallbladder cancer [GBC]) 177 cases of HCC, 58 cases of IBDC and 210 cases of EBDSC, including 76 cases of GBC	WC and WHR—extreme tertiles Waist-to-height ratio (WHtR)—extreme tertiles	All anthropometric measures were positively associated with risk of HCC and GBC. WHtR HCC RR = 3.51 (2.09–5.87) GBC RR = 1.56 (1.12–2.16) No association was observed between abdominal obesity and risk of IBDC and EBDSC.	Overall WC—risk WHtR—risk WC and WHR—NS (IBDC and EBDSC)
Gaudet (2015)[49]	20 cohort studies Pooled data from 1 941 300 participants, including 3760 cases	Head and neck cancer	WC per 5 cm: WHR per 0.1 unit HC	After adjustment for BMI WC HR = 1.04 (1.03–1.05) WHR HR = 1.07 (1.05–1.09) Larger HC was not associated.	Overall WC—risk WHR—risk HC—NS
Kitahara (2016)[50]	Pooled analysis of 22 prospective studies	Thyroid cancer	WC (per 5 cm)	HR = 1.03 (1.01–1.05)	Overall WC—risk
Aune (2015)[45]	Systematic review and meta-analysis of prospective studies	Ovarian cancer	WC per 10 cm HC WHR	WC RR = 1.06 (1.00–1.12) HC and WHR—not association	Overall WC—NS HC—NS

(Continues)

TABLE 1 (Continued)

Author/year	Design Population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
					WHR—NS
Hidayat (2016)[48]	Meta-analyses of observational studies	Lung cancer	WC—10-cm increase WHR—0.1-unit increase	WC RR = 1.10 (1.04–1.17) WHR RR = 1.05 (1.00–1.11) Highest versus lowest categories: WC RR = 1.32 (1.13–1.54) WHR RR = 1.10 (1.00–1.23) WC Never smokers RR = 1.11 (1.00–1.23) Former smokers RR = 1.12 (1.03–1.22) Current smokers RR = 1.16 (1.08–1.25)	Overall WC—Risk
Abar (2019)[62]	Meta-analysis of prospective studies	Lymphohaematopoietic cancers	WC WHR	Higher WC—no associated with multiple myeloma WHR associated with diffuse large β-cell lymphoma	WC—NS WHR—risk

TABLE 2 Epidemiological evidence on the association between visceral obesity and incident cardiovascular disease in adults and/or older adults

Author/year	Design population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
Anthropometric measures—All sample					
Chan (2007)[28]	Case control study Hong Kong, China Presence of CAD (n = 206) Control group general population (n = 207)	Coronary artery disease	WC ≥ 91.4 cm for men or ≥81.3 cm for women	WC OR = 2.29 (1.29–3.72)	WC Overall—risk
The Emerging Risk Factors Collaboration (2011)[53]	Cohort—collaborative analysis of 58 prospective studies 221 934 people in 17 countries 14 297 incident cardiovascular disease outcome	First-onset cardiovascular disease	WC WHR	After adjustment: WC HR = 1.10 (1.05–1.14) WHR HR = 1.12 (1.08–1.15)	Overall WC—risk WHR—risk
van Wijk (2016)[51]	Cohort—European Prospective Investigation of Cancer–Norfolk 7279 participants EPIC-Norfolk—10-country collaborative EPIC study	Coronary heart disease	WC ≥ 102 cm in men and ≥89 cm in women	Stratified by C-reactive protein levels (≥2 mg L^{-1}) WC HR = 1.38 (1.08–1.75)	WC Overall—risk
Feliciano (2017)[22]	Cohort—population of Kaiser Permanente Northern California (KPNC) 3109 early-stage breast cancer (stage I–III) 18 to 80 years without pre-existing CVD Follow-up 8.28 years	Cardiovascular disease (CVD) among breast cancer patients	WC—comparing 100 vs. 80 cm	HR: 1.93 (1.31–2.84) WC increased risk of CVD, independent of pre-existing risk factors.	WC Women—risk
Aune (2016)[56]	Systematic review and meta-analysis of prospective studies 23 prospective studies >15 905 incident cases 647,388 participants	Heart failure	WC—10-cm increase WHR—0.1-unit increase	WC RR = 1.29 (CI 1.21–1.37) WHR RR = 1.29 (CI 1.13–1.47)	Overall WC—risk WHR—risk
Anthropometric measures—Sex-specific and BMI class analyses					
Li (2006)[52]	Prospective population-based study, Malmo, Sweden 7 years follow-up 10 369 men and 16 638 women 45–73 years old	Incidences of first-cardiac event (CE) and ischemic stroke	WHR Cut-off points for tertiles of WHR	WHR after adjustments Men Normal weight RR = 1.24 (1.13–1.37) Overweight RR = 1.06 (0.94–1.20) Obesity RR = 1.04 (0.87–1.24) Women Normal weight RR = 1.24 (1.11–1.39) Overweight RR = 1.31 (1.18–1.46) Obesity RR = 1.27 (1.07–1.51)	WHR Men—risk in normal weight Men—NS in overweight Women—risk in normal end overweight
Carlsson (2013)[54]	Population-based study—the Malmö	Cardiovascular disease	WC WHR	CVD risk factor-adjusted:	Men WC—NS

(Continues)

TABLE 2 (Continued)

Author/year	Design population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
	Diet and Cancer study-cardiovascular cohort 1751 men and 1990 women, aged 60 years without CVD at baseline 11 years of follow-up		Waist-hip-height ratio (WHHR) WC-to-height ratio (WCHR) SAD-to-height ratio (SADHR) Sagittal abdominal diameter (SAD)	Men WC, WHR and WCHR were not associated SAD 1.16 (1.02–1.30 WHHR 1.19 (1.05–1.36) SADHR 1.19 (1.07–1.32) Women Only WHHR 1.20 (1.01–1.43) was associated	WHR NS WCHR—NS SAD—risk WHHR—risk SADHR—risk Women WC—NS WHR NS WCHR—NS SAD—NS WHHR—risk SADHR—NS
Carlsson (2014)[55]	Cohort *N* 3741 (53% women) 60-year old without CVD followed for 11-years	CVD All cases of fatal and nonfatal	WHR WC Sagittal abdominal diameter (SAD) Waist-hip-height ratio (WHHR)	Women normal weight (BMI < 25) WHR 1.91 (1.35–2.70) WC 1.81 (1.02–3.20) SAD 1.25 (0.74–2.11) WHHR 1.97 (1.40–2.78) Men normal weight (BMI < 25) WHR, WHHR and WC were not associated SAD only associated CVD HR = 1.19 (1.04–1.35) Adjustments for established risk factors. Women overweight/obese None of the measures were significantly associated. Men overweight/obese All measures were significant predictors WHR 1.24 (1.04–1.47) WC 1.19 (1.00–1.42) SAD 1.21 (1.00–1.46) WHHR 1.23 (1.05–1.44).	Women normal weight WHR—risk WC—risk SAD—risk WHHR—risk Women overweight WHR—NS WC—NS SAD—NS WHHR—NS Men normal weight WHR—NS WC—NS SAD—risk WHHR—NS Men overweight WHR—risk WC—risk SAD—risk WHHR—risk
Body composition variables					
Fox (2007)[21]	Framingham Heart Study—population-based 3001 participants free of clinical cardiovascular disease Mean age 50 years	Systolic and diastolic blood pressure (SBP) and (DBP)	Visceral adipose tissue (VAT) Measured by computed tomography	VAT was associated with SBP and DBP ($p \leq 0.0001$) in men and women	VAT Overall—risk
Mahabadi (2009)[57]	Framingham Heart Study Offspring cohort 1267 participants Mean age 60 years	Prevalence of cardiovascular disease (CVD).	VAT by computed tomography	VAT OR = 1.23 (0.92–1.63) adjustment for traditional risk factor	VAT Overall—NS
Britton (2013)[6]	Cohort Framingham Heart Study *n* = 3086, 49% women, mean age 50.2 years	Incident cardiovascular disease	VAT by computed tomography	VAT HR 1.44 (1.08–1.92) By sex VAT	VAT Overall—risk Women—NS Men—risk

TABLE 2 (Continued)

Author/year	Design population	Outcome	Visceral obesity measurement	Visceral obesity results	Summary
	Followed up 5.0 years			Women 1.04 (0.65–1.65) Men 1.66 (1.16–2.39)	
Kouli (2017)[59]	Prospective study in Europe—ATTICA study 3,042 adults 10 years follow-up	Fatal/nonfatal CVD incidence	Visceral adiposity index (VAI)by CT	After adjusting for multiple confounders, VAI OR = 1.05 (1.01–1.10) Men HR = 1.06 (1.00–1.11) Women HR = 1.06 (0.96–1.10)	VAI Overall—risk Women—NS Men—NS
Body composition and anthropometric measures					
Nicklas (2004)[60]	Health, Ageing and Body Composition Study Follow-up 4.6 years Men (*n* = 1,116), women (n = 1,387) Aged 70–79 years	Incident myocardial infarction (MI) Fatal or nonfatal	WC waist-to-thigh ratio (WTR) VAT (per 66.23-cm^2 increase) VAT/SAT (per 0.30 increase) VAT/fat mass (per 2.17 increase) Computed tomography	Women WC and WTR were not associated VAT HR = 1.67 (1.28–2.17) VAT/SAT area HR = 1.42 (1.08–1.87) VAT/fat mass HR = 1.67 (1.20–2.31) Men No association were observed WC, WTR, VAT and VAT/SAT	Women WC—NS WTR—NS VAT—risk VAT/SAT—risk VAT/fat mass—risk Men WC—NS WTR—NS VAT—NS VAT/SAT—NS VAT/fat mass—NS
Jasper (2017)[58]	'SMART' cohort—secondary manifestations of arterial disease Follow-up 6.8 years, 1767 patients, 18–79 years old	Vascular events Fatal or nonfatal	WC VAT%—visceral fat to total abdominal fat measured by ultrasound	WC Men HR = 1.13 (CI 0.97–1.32) Women HR = 1.00 (CI 0.76–1.32) VAT% HR = 1.15 (0.99–1.34)	WC Men—NS Women—NS VAT—NS

between overall cancer with body composition variables, visceral adipose tissue (VAT) and trunk-to-peripheral fat (TPF) ratio using computed tomography (CT) and body dual-energy X-ray (DXA) (Table 1). In both cohorts, VAT and TPF, after adjustment for clinical risk factors and BMI, were associated to overall cancer risk in all participants. However, this association remained significant only among men after stratification by sex. The European cohort[23] also found that respiratory and gynaecological cancer were associated with abdominal obesity, whereas gastrointestinal cancer was not. In contrast, a cohort with Chinese women that analysed overall cancer, ovarian, endometrial and postmenopausal breast cancer did not find an association with visceral obesity measured by WHR.[24] An umbrella review[16] that analysed 36 cancer sites using WC and WHR as visceral obesity measures found the following associations: WC and WHR with colon cancer in all participants, men and women; WC and WHR with pancreatic and endometrial cancer; and WC with ovarian cancer. The other 32 cancer sites were not associated with visceral obesity measured by WC and WHR, which may be a consequence of multiple test corrections, because studies investigating the association between visceral adiposity and each cancer site separately showed more positive associations.

Several studies analysed the association between colorectal cancer and visceral obesity using body composition,[25,26] anthropometric measures such as WC and WHR[27,28] or both[29,30] methods (Table 1). An increase in visceral adiposity was associated with colorectal adenoma risk in the general healthy population.[30] These studies, including a meta-analysis of 12 observational studies, found an association between colorectal adenoma and colorectal cancer with visceral obesity measured by VAT or visceral fat area.[25,26,29,30] In this meta-analysis, every 25-cm^2 increase of VAT resulted in 13% more risk of colorectal adenoma. Visceral obesity measured by WC was associated in some studies[28,30] but not in others[29] with colorectal cancer. A recent systematic review of prospective studies[27] found a positive association between colorectal cancer and WC and between colorectal adenoma and WHR. There is clear evidence linking visceral obesity measured by body composition or anthropometric measures to

colorectal cancer. Based on the existing evidence, the World Cancer Research Fund (WCRF) and the American Institute of Cancer have classified body fatness as a risk factor for colorectal cancer.[31]

The evidence for the association between prostate cancer and visceral obesity show conflicting results. WC and WHR were associated with prostate cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) study, including data from eight countries.[17] However, a study using data from Italian men with moderate to high cardiovascular risk did not find an association between WC and prostate cancer.[18] In a Canadian case–control study, WC was a protective factor to prostate cancer after adjustment for potential confounders (OR = 0.70 [0.60–0.82]).[10] Prostate cancer and its association with visceral obesity have been evaluated only by anthropometric measures such as WC and WHR and the data are still very controversial. In line with this, the WCRF classified as 'probable' the current evidence for the association between body fatness, including WC and WHR measures, and prostate cancer.[31] There is still no evidence of an association between visceral obesity and prostate cancer.

Globally, breast cancer is the most incident type of cancer in women. The overall prevalence of obesity, measured by BMI, is also the highest in women. The association between breast cancer and visceral adiposity has been investigated in several studies using anthropometric measures such as WC and WHR, that is, the ORDET cohort, EPIC, AMBER Consortium, Sister Study and a meta-analysis.[11,19,32–34] In premenopausal women, breast cancer was not associated with WC,[11,19,32,34] only with WHR in Estrogen receptor-positive tumours.[33] Similarly, a meta-analysis and the Sister Study,[11,34] which stratified analyses by body status, WC and WHR were not associated with premenopausal breast cancer. On the other hand, in postmenopausal women, although WC was not associated in two studies,[19,32] a meta-analyses found a positive association,[11] despite the small magnitude of the effect (RR = 1.06 [1.04–1.09]). In the Sister Study, the most recent study and with the largest sample investigating this topic, WC and WHR were associated with breast cancer in postmenopausal women classified as normal or overweight/with obesity..[34] Like other well-known risk factors for breast cancer, there are also differences between postmenopausal and premenopausal risk for visceral obesity. These results suggest that high WC and WHR are not important risk factors for breast cancer among premenopausal but increase considerably the risk in postmenopausal despite overall adiposity.

The associations between endometrial cancer and visceral adiposity, assessed by WC, WHR and HC, were positive in all studies including an umbrella review.[12,35,36] The exception was the Black Women's Health Study,[37] a cohort of almost 48 000 black women, which did not find an association between endometrial cancer and WHR, WC or HC. Similarly to the findings with breast cancer, visceral obesity was associated with increased risk of endometrial cancer in postmenopausal women independently of their BMI.[23,34,35,38]

Pancreatic cancer was also positively associated with visceral obesity, measured by WC and WHR, in a systematic review.[13,39] Similar association was observed for WHR but not for WC in the Women's Health Initiative study.[40] There is strong evidence suggesting that visceral obesity increases the risk of pancreatic cancer. However, it is important to conduct sex-specific analyses to support such evidence.

Regarding gastro-oesophageal cancer, a systematic review showed that higher WC and WHR were associated with all subtypes of gastric and oesophageal cancers[14,41] even after adjustment for BMI.[42] HP does not show the same association probably because it does not measure visceral fat but obesity pear-shaped body, that is, more fat tissue around the hips than in the abdomen itself.

The association between renal and visceral adiposity shows conflicting results. Renal cancer was found to be associated in postmenopausal women with WHR[15] and with WC in the EPIC study.[43] Among men, visceral obesity measured by WC, WHR and HC were not associated to renal cancer. However, a recent article showed a positive association between WC and kidney cancer in 23.3 million East Asians.[44]

There is also some evidence on the association between other types of cancer such as ovarian,[45] hepatocellular, gallbladder, intrahepatic/extrahepatic bile duct system,[46] bladder and urothelial,[20] Hodgkin's lymphoma, multiple myeloma,[47] lung,[48] head and neck cancer[49] and visceral adiposity. All these studies used conventional anthropometric measures, that is, WC, WHR and HC, and also included new ones such as waist-to-height ratio (WHtR).[46] However, none had included body composition variables. WC was positively associated with ovarian,[45] hepatocellular carcinoma,[46] gallbladder cancer,[20,46] urothelial carcinoma of the bladder,[20] lung,[48] head and neck[49] and thyroid cancer,[50] whereas WHR was associated with hepatocellular carcinoma,[46] gallbladder cancer,[46] head and neck[49] and lung cancer,[48] even after adjustment for smoking status. Visceral obesity evaluated by WC was no associated with intrahepatic extrahepatic bile duct system,[46] Hodgkin's lymphoma and multiple myeloma.[47] WHtR was strongly associated with hepatocellular carcinoma.[46] The identification of visceral obesity risk in several types of cancer is important in order to determine the specific targets of preventive public health programs.

3.2 | Evidence of visceral obesity on incident CVD

Obesity is a well-known risk factor of CVD in adults, and in this section, we investigate the evidence on visceral obesity and CVD. Most studies included in this review article had used anthropometric measures, mainly WC and WHR, to evaluate the association between CVD risk and visceral obesity[22,28,51–56] (Table 2). There were studies that used body composition measured by computed tomography, DXA or ultrasound.[6,57–59] VAT is the most used body composition variable to describe visceral fat. Fewer studies had used both methods to analyse visceral obesity.[28,58]

A positive association between WC and WHR with CVD risk (heart failure, coronary artery disease or CVD risk factor) was found in few cohort studies and in a systematic review.[22,28,51,53,56] However, in three cohort studies that performed sex-specific analyses, the association between WC and myocardial infarction[60] or CVD risk[54,58] disappeared in women and not significant in men. A similar pattern was

observed for WHR and CVD risk, which was not associated in both sexes.[54] The findings, however, from cohort studies that analysed visceral obesity with more sophisticated methods of body composition, such as computed tomography, the variables VAT or visceral adiposity index (VAI) were associated with CVD[6,21,58–60] in all participants. However, when the analysis was stratified by sex, VAT remained associated with blood pressure risk[21] in both men and women, but it was not associated with CVD risk in women[6,59] in two cohorts.

In addition to the importance of sex-specific analyses in understanding the association between CVD risk and visceral obesity using anthropometrics or body composition methods, the influence of ageing should also be considered. The Health, Aging and Body Composition Study[60] with individuals aged 70 and older did not find an association for WC and myocardial infarction risk in both men and women. However, they found an association with VAT in all participants. In contrast, in the Framingham Heart Study Offspring cohort,[57] mean age was 60 years old; VAT was not associated with CVD risk. The impact of visceral obesity in CVD remains controversial in older adults.

Other significant question is about the influence of nutritional status in visceral obesity associated with incident CVD. It is also important to stratified data by nutritional body status and sex. A Swedish cohort[52] stratified their analyses of WHR by sex and BMI and found that the highest tercile of WHR was associated with CVD in women independent of BMI class and in men only among those classified as normal weight. In contrast, another cohort[55] found that WC and WHR were associated with CVD only among women with normal BMI and in overweight and men with obesity.

In most studies, visceral obesity was defined based on anthropometric measurements, but with variations in their anthropometric assessment methods, mainly anatomical points used and different cut-off points. These differences across studies can affect the accuracy and comparisons between them as well as the understanding of which specific body size measures, that is, WC or WHR better identifies those at high risk for different types of cancer. There is also evidence of several sex-specific associations between visceral obesity and several types of cancer that used sex-specific cut-offs sometimes and did not other times. Regarding the anatomical points, we observed a great variation in measurements for WC: narrowest point between the iliac crest and the lower rib,[32] midpoint between the lowest rib and the top of the iliac crest[34,54,55,58] and narrowest torso circumference[43] 2 cm above umbilicus.[20] It is important to use standard measures and cut-offs for the same anatomical point to improve results.

The anthropometric measurements were the most widely used methods to define abdominal obesity, that is, WC and WHR. On one hand, this is a positive aspect because they are the most accessible and cheaper methods to be used in clinical settings and in the general population compared with body composition methods. However, the specific body composition components are more relevant to understand how the visceral obesity can affect both CVD and cancer risks. Body composition methods are more accurate than a single anthropometric measurement to assess the components of visceral obesity: SAT and VAT. WC reflects both.

4 | CONCLUSIONS AND FUTURE RESEARCH

This integrative review aimed to investigate further the role of visceral obesity on incident cancer and CVD. The impact of visceral obesity on CVD is overall clear in adults but remains controversial by sex, age and BMI categories, regardless the method used to measure visceral obesity. The predictive capacity of different visceral obesity variables needs further investigation. Moreover, visceral obesity can increase the risk of some specific cancer types, but there were controversial findings about CVD risk according to sex specific and in older adults varying with different measures used such as WC and VAT. There is enough evidence showing that visceral obesity increases the risk of colorectal, pancreatic and gastro-oesophageal cancer. However, for some types of cancer such as breast and endometrial, visceral obesity is a risk only in postmenopausal women. Regarding prostate and renal cancer, the evidence is still unclear, and there is a need for more studies. For certain cancers, such as postmenopausal breast and endometrial cancers, it was observed that visceral obesity increased their risk regardless overall individual's BMI.

Despite the evidence on visceral obesity showing an association with CVD risk, this association disappears in sex-specific analyses and in older adults. The link between visceral obesity and CVD risk remains unclear because sex differences, changes with ageing and BMI category can modify it. Therefore, further epidemiological studies with analyses stratified by sex and samples including older adults aged 65 and older are needed.

CONFLICT OF INTEREST

No conflict of interest was declared.

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REFERENCES

1. World Health Organization. *Global Strategy on Diet, Physical Activity and Health*. WHO Press: Geneva (Switzerland); 2008.
2. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer—viewpoint of the IARC Working Group. *N Engl J Med*. 2016; 375(8):794-798.
3. Caleyachetty R, Thomas GN, Toulis KA, et al. Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. *J am Coll Cardiol*. 2017;70(12):1429-1437.
4. World Health Organization. *Global Action Plan for the Prevention and Control of Noncommunicable Diseases (2013-2020)*. Geneva (Switzerland): WHO Press; 2013.
5. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*. Report of a WHO consultation. Geneva (Switzerland): WHO Press, 2000.
6. Britton KA, Massaro JM, Murabito JM, Kreger BE, Hoffmann U, Fox CS. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. *J Am Coll Cardiol*. 2013;62(10):921-925.

7. Doyle SL, Donohoe CL, Lysaght J, Reynolds JV. Visceral obesity, metabolic syndrome, insulin resistance and cancer. *Proc Nutr Soc*. 2012; 71(1):181-189.
8. Liu J, Fox CS, Hickson DA, et al. Impact of abdominal visceral and subcutaneous adipose tissue on cardiometabolic risk factors: the Jackson Heart Study. *J Clin Endocrinol Metab*. 2010;95(12):5419-5426.
9. Bonneau GA, Pedrozo WR, Berg G. Adiponectin and waist circumference as predictors of insulin-resistance in women. *Diabetes Metab Syndr Clin Res Rev*. 2014;8:3-7.
10. Blanc-Lapierre A, Spence A, Karakiewicz PI, Aprikian A, Saad F, Parent MÉ Metabolic syndrome and prostate cancer risk in a population-based case-control study in Montreal, Canada. Chronic Disease Epidemiology. *BMC Public Health* 2015; 15: 1–11.
11. Chen G-C, Chen S-J, Zhang R, et al. Central obesity and risks of pre- and postmenopausal breast cancer: a dose-response meta-analysis of prospective studies. *Obes Rev*. 2016;17(11):1167-1177.
12. Aune D, Navarro Rosenblatt DA, Chan DSM, et al. Anthropometric factors and endometrial cancer risk: a systematic review and dose-response meta-analysis of prospective studies. *Ann Oncol*. 2015;26 (8):1635-1648.
13. Aune D, Greenwood DC, Chan DSM, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and nonlinear dose–response meta-analysis of prospective studies. *Ann Oncol*. 2012;23(4):843-852.
14. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. *Biosci Rep*. 2017;37:BSR20160474.(3):
15. Luo J, Margolis KL, Adami H-O, et al. Body size, weight cycling, and risk of renal cell carcinoma among postmenopausal women: the Women's Health Initiative (United States). *Am J Epidemiol*. 2007;166 (7):752-759.
16. Kyrgiou M, Kalliala I, Markozannes G, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. *BMJ*. 2017; 356:1-10.
17. Pischon T, Boeing H, Weikert S, et al. Body size and risk of prostate cancer in the European Prospective Investigation into Cancer and Nutrition. *Cancer Epidemiol Biomarkers Prev*. 2008;17(11):3252-3261.
18. De Nunzio C, Truscelli G, Trucchi A, et al. Metabolic abnormalities linked to an increased cardiovascular risk are associated with high-grade prostate cancer: a single biopsy cohort analysis. *Prostate Cancer Prostatic Dis*. 2016;19(1):35-39.
19. Agnoli C, Grioni S, Sieri S, et al. Metabolic syndrome and breast cancer risk: a case-cohort study nested in a multicentre Italian cohort. *PLoS One*. 2015;10:1-12.
20. Montella M, Di Maso M, Crispo A, et al. Metabolic syndrome and the risk of urothelial carcinoma of the bladder: a case-control study. *BMC Cancer*. 2015;15:1-7.
21. Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments. *Circulation*. 2007;116(1): 39-48.
22. Cespedes Feliciano EM, Kwan ML, Kushi LH, Weltzien EK, Castillo AL, Caan BJ. Adiposity, post-diagnosis weight change, and risk of cardiovascular events among early-stage breast cancer survivors. *Breast Cancer Res Treat*. 2017;162(3):549-557.
23. Staunstrup LM, Nielsen HB, Pedersen BK, et al. Cancer risk in relation to body fat distribution, evaluated by DXA-scans, in postmenopausal women—the prospective epidemiological risk factor (PERF) study. *Sci Rep*. 2019;9(1):5379.
24. Liu Y, Warren Andersen S, Wen W, et al. Prospective cohort study of general and central obesity, weight change trajectory and risk of major cancers among Chinese women. *Int J Cancer*. 2016;139(7): 1461-1470.
25. Yamaji T, Iwasaki M, Sasazuki S, et al. Visceral fat volume and the prevalence of colorectal adenoma. *Am J Epidemiol*. 2009;170(12): 1502-1511.
26. Keum NN, Lee DH, Kim R, Greenwood DC, Giovannucci EL. Visceral adiposity and colorectal adenomas: dose-response meta-analysis of observational studies. *Ann Oncol*. 2015;26(6):1101-1109.
27. Abar L, Vieira AR, Aune D, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF–AICR systematic review of published prospective studies. *Eur J Nutr*. 2018;57(5):1701-1720.
28. Chan AOO, Jim MH, Lam KF, et al. Prevalence of colorectal neoplasm among patients with newly diagnosed coronary artery disease. *JAMA*. 2007;298(12):1412-1419.
29. Oh T-HH, Byeon J-SS, Myung S-JJ, et al. Visceral obesity as a risk factor for colorectal neoplasm. *J Gastroenterol Hepatol*. 2008;23(3): 411-417.
30. Kang HW, Kim D, Kim HJ, et al. Visceral obesity and insulin resistance as risk factors for colorectal adenoma: a cross-sectional, case-control study. *Am J Gastroenterol*. 2010;105(1):178-187.
31. World Cancer Reserch Fund. The cancer process, https://www.wcrf.org/dietandcancer/resources-and-toolkit (2018).
32. Agnoli C, Berrino F, Abagnato CA, et al. Metabolic syndrome and postmenopausal breast cancer in the ORDET cohort: a nested case-control study. *Nutr Metab Cardiovasc Dis*. 2010;20(1):41-48.
33. Bandera EV, Chandran U, Hong C-C, et al. Obesity, body fat distribution, and risk of breast cancer subtypes in African American women participating in the AMBER Consortium. *Breast Cancer Res Treat*. 2015;150(3):655-666.
34. Park YMM, White AJ, Nichols HB, O'Brien KM, Weinberg CR, Sandler DP. The association between metabolic health, obesity phenotype and the risk of breast cancer. *Int J Cancer*. 2017;140(12): 2657-2666.
35. Reeves KW, Carter GC, Rodabough RJ, et al. Obesity in relation to endometrial cancer risk and disease characteristics in the Women's Health Initiative. *Gynecol Oncol*. 2011;121(2):376-382.
36. Raglan O, Kalliala I, Markozannes G, et al. Risk factors for endometrial cancer: an umbrella review of the literature. *Int J Cancer*. 2019;145(7): 1719-1730.
37. Sponholtz TR, Palmer JR, Rosenberg L, Hatch EE, Adams-Campbell LL, Wise LA. Body size, metabolic factors, and risk of endometrial cancer in black women. *Am J Epidemiol*. 2016;183(4): 259-268.
38. Amankwah EK, Friedenreich CM, Magliocco AM, et al. Anthropometric measures and the risk of endometrial cancer, overall and by tumor microsatellite status and histological subtype. *Am J Epidemiol*. 2013; 177(12):1378-1387.
39. Genkinger JM, Spiegelman D, Anderson KE, et al. A pooled analysis of 14 cohort studies of anthropometric factors and pancreatic cancer risk. *Int J Cancer*. 2011;129(7):1708-1717.
40. Luo J, Margolis KL, Adami H-O, LaCroix A, Ye W, Women's Health Initiative Investigators. Obesity and risk of pancreatic cancer among postmenopausal women: the Women's Health Initiative (United States). *Br J Cancer*. 2008;99(3):527-531.
41. O'Doherty MG, Freedman ND, Hollenbeck AR, Schatzkin A, Abnet CC. A prospective cohort study of obesity and risk of oesophageal and gastric adenocarcinoma in the NIH–AARP Diet and Health Study. *Gut*. 2012;61(9):1261-1268.
42. Steffen A, Huerta J-M, Weiderpass E, et al. General and abdominal obesity and risk of esophageal and gastric adenocarcinoma in the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer*. 2015;137(3):646-657.
43. Pischon T, Lahmann PH, Boeing H, et al. Body size and risk of renal cell carcinoma in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Int J Cancer*. 2006;118(3):728-738.
44. Nam GE, Cho KH, Han K, et al. Obesity, abdominal obesity and subsequent risk of kidney cancer: a cohort study of 23.3 million east Asians. *Br J Cancer*. 2019;121(3):271-277.
45. Aune D, Navarro Rosenblatt DA, Chan DSM, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear

dose-response meta-analysis of prospective studies. *Int J Cancer*. 2015;136(8):1888-1898.
46. Schlesinger S, Aleksandrova K, Pischon T, et al. Abdominal obesity, weight gain during adulthood and risk of liver and biliary tract cancer in a European cohort. *Int J Cancer*. 2013;132(3):645-657.
47. Britton JA, Khan AE, Rohrmann S, et al. Anthropometric characteristics and non-Hodgkin's lymphoma and multiple myeloma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Haematologica*. 2008;93(11):1666-1677.
48. Hidayat K, Du X, Chen G, Shi M, Shi B. Abdominal obesity and lung cancer risk: systematic review and meta-analysis of prospective studies. *Nutrients*. 2016;8(12):810.
49. Gaudet MM, Kitahara CM, Newton CC, et al. Anthropometry and head and neck cancer: a pooled analysis of cohort data. *Int J Epidemiol*. 2015;44(2):673-681.
50. Kitahara CM, McCullough ML, Franceschi S, et al. Anthropometric factors and thyroid cancer risk by histological subtype: pooled analysis of 22 prospective studies. *Thyroid*. 2016;26(2):306-318.
51. van Wijk DF, Boekholdt SM, Arsenault BJ, et al. C-reactive protein identifies low-risk metabolically healthy obese persons: the European prospective investigation of Cancer-Norfolk prospective population study. *J am Heart Assoc*. 2016;5:1-8.
52. Li C, Engström G, Hedblad B, Calling S, Berglund G, Janzon L. Sex differences in the relationships between BMI, WHR and incidence of cardiovascular disease: a population-based cohort study. *Int J Obes (Lond)*. 2006;30(12):1775-1781.
53. The Emerging Risk Factors Collaboration. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet*. 2011;377:1085-1095.
54. Carlsson AC, Risérus U, Engström G, et al. Novel and established anthropometric measures and the prediction of incident cardiovascular disease: a cohort study. *Int J Obes (Lond)*. 2013;37(12):1579-1585.
55. Carlsson AC, Riserus U, Ärnlöv J, et al. Prediction of cardiovascular disease by abdominal obesity measures is dependent on body weight and sex—results from two community based cohort studies. *Nutr Metab Cardiovasc Dis*. 2014;24(8):891-899.
56. Aune D, Sen A, Norat T, et al. Body mass index, abdominal fatness, and heart failure incidence and mortality. *Circulation*. 2016;133(7):639-649.
57. Mahabadi AA, Massaro JM, Rosito GA, et al. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. *Eur Heart J*. 2009;30(7):850-856.
58. Jaspers NEM, Dorresteijn JAN, Van Der Graaf Y, et al. Relation between adiposity and vascular events, malignancy and mortality in patients with stable cerebrovascular disease. *Int J Obes (Lond)*. 2017;41(12):1775-1781.
59. Kouli G-M, Panagiotakos DB, Kyrou I, et al. Visceral adiposity index and 10-year cardiovascular disease incidence: the ATTICA study. *Nutr Metab Cardiovasc Dis*. 2017;27(10):881-889.
60. Nicklas BJ, Penninx BWJH, Cesari M, et al. Association of visceral adipose tissue with incident myocardial infarction in older men and women: the health, aging and body composition study. *Am J Epidemiol*. 2004;160(8):741-749.
61. Lee KR, Seo MH, Do Han K, Jung J, Hwang IC, Taskforce Team of the Obesity Fact Sheet of the Korean Society for the Study of Obesity. Waist circumference and risk of 23 site-specific cancers: a population-based cohort study of Korean adults. *Br J Cancer*. 2018;119(8):1018-1027.
62. Abar L, Sobiecki JG, Cariolou M, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. *Ann Oncol*. 2019;30(4):528-541.

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